UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/559,984	04/26/2000	Jeffrey A. Hubbell	50166/002001	1784

21559 7590 09/26/2003

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER
DI NOLA BARON, LILIANA

ART UNIT	PAPER NUMBER
1615	21

DATE MAILED: 09/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/559,984	Applicant(s) HUBBELL ET AL.	
	Examiner Liliana Di Nola-Baron	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of Applicant's amendment, filed on July 14, 2003, is acknowledged.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1- 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parker et al. (U.S. Patent 6,218,464) in view of Jodal et al.

Parker et al. provides a method for preparing a fluorinated emulsion polymer comprising mixing the monomer mixture with a macromolecular organic compound, such as cyclodextrin and cyclodextrin derivatives (See col. 2, lines 1-17 and col. 4, lines 41-60). The monomer mixture disclosed by Parker et al. comprises one monomer having high water solubility attached to one fluorinated monomer and to one non-fluorinated monomer having low water solubility (See col. 2, lines 9-15). Thus, the polymer disclosed by the patent comprises a water-soluble domain with at least two hydrophobic interacting groups, as claimed by Applicant. The examples 1-6 provided in the patent and Table 1 show that the use of cyclodextrin in the emulsion polymerization of fluorinated polymers reduces the amount of gel formed during polymerization.

Thus, Parker et al. provides the general teachings that addition of cyclodextrin to fluorinated polymers prevents gel formation. Parker et al. is deficient in the fact, that it does not include a step for the hydrolysis of cyclodextrin in the method of the invention.

Jodal et al. discloses enzymatic degradation of cyclodextrin with α-amylase (See Introduction and Discussion).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the hydrogel precursors disclosed by Parker et al., by including a molecule, such as an α-amylase, to disrupt the interaction between the polymer and cyclodextrin, as taught by Jodal et al. The expected result would have been a successful hydrogel composition and a successful method of forming said composition. Because of the teachings of Parker et al., that addition of cyclodextrin to solutions comprising fluorinated polymers reduces or eliminates gel formation, and the teachings of Jodal et al., that cyclodextrin may be enzymatically degradated, one of ordinary skill in the art would have a reasonable expectation that the compositions and methods claimed in the instant application would be successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

3. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Parker et al. in view of Jodal et al., as applied to claims 1-14 above, and further in view of Rhee et al. (U.S. Patent 5,324,775).

The teachings of Parker et al. and Jodal et al. have been summarized above.

Rhee et al. discloses biocompatible compositions, formed by covalently binding natural inert polymers to synthetic hydrophilic polymers, such as polyethylene glycol (See col. 2, lines 1-8). Rhee et al. includes dextrins, such as cyclodextrin, among the natural polymers used in the invention and teaches that the compositions may include active proteins, such as cytokines (See col. 2, lines 9-27). Rhee et al. teaches that the compositions are formulated in a flowable form and injected into the patient, and after injection, the carrier is removed (See col. 2, lines 48-59). Rhee et al. teaches that in order to form the conjugates of the invention, the hydrophilic polymer, specifically PEG, is functionalized by various methods (See col. 10, lines 3-38).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the hydrogel precursors disclosed by Parker et al., by including a biological agent, such as a protein, to device a method to deliver active agents into a tissue. The expected result would have been a successful method for incorporating an active agent in a hydrogel composition. Because of the teachings of Rhee et al., that compositions comprising synthetic polymers and cyclodextrin may incorporate active agents, one of ordinary skill in the art would have a reasonable expectation that the method claimed in the instant application would

be successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

4. Claims 15, 16 and 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harmer et al. (U.S. Patent 6,281,400) in view of Rhee et al.

Harmer et al. provides a process comprising preparing a liquid composition of a fluorinated polymer and removing the organic solvent by techniques known in the art (See col. 3, lines 1-26). Harmer et al. teaches that gelation of the composition comprising the fluorinated polymer occurs only after removal of the organic solvent (See col. 5, line 52 to col. 6, line 28). Thus, Harmer et al. provides the general teachings, that fluorinated polymers may be mixed with organic solvents and gel formation occurs only after removal of the organic solvent from the solution. Harmer et al. does not specifically teach that the hydrogel can be formed in contact with a tissue and may incorporate an active agent.

Rhee et al. discloses biocompatible compositions, formed by covalently binding natural inert polymers to synthetic hydrophilic polymers, such as polyethylene glycol (See col. 2, lines 1-8). Rhee et al. includes dextrins, such as cyclodextrin, among the natural polymers used in the invention and teaches that the compositions may include active proteins, such as cytokines (See col. 2, lines 9-27). Rhee et al. teaches that the compositions are formulated in a flowable form and injected into the patient, and after injection, the carrier is removed (See col. 2, lines 48-59).

Rhee et al. teaches that in order to form the conjugates of the invention, the hydrophilic polymer, specifically PEG, is functionalized by various methods (See col. 10, lines 3-38).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the hydrogel precursors disclosed by Harmer et al., by including a biological agent, such as a protein, to device a method to deliver active agents into a tissue. The expected result would have been a successful method for incorporating an active agent in a hydrogel composition. Because of the teachings of Rhee et al., that compositions comprising synthetic polymers and cyclodextrin may incorporate active agents, one of ordinary skill in the art would have a reasonable expectation that the method claimed in the instant application would be successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

5. Applicant's arguments filed on July 14, 2003 have been fully considered but they are have been found only partially persuasive.

6. Applicant's argument with respect to the 35 U.S.C. 112, second paragraph rejection of the previous Office action have been found persuasive, since Applicant's specification teaches mechanisms of interaction between different groups and destruction of said interactions. Accordingly, said rejection is withdrawn.

7. Applicant argues that the polymers disclosed by Parker et al. do not contain a water-soluble domain and the copolymer is mostly hydrophobic. In response to said argument, it is noted that the monomer mixture disclosed by Parker et al. comprises one monomer having high water solubility attached to one fluorinated monomer and to one non-fluorinated monomer having low water solubility (See col. 2, lines 9-15). Thus, the polymer disclosed by the patent comprises a water-soluble domain with at least two hydrophobic interacting groups, as claimed by Applicant. Furthermore, Applicant's claimed invention is directed to a polymer comprising a water-soluble polymer domain, and not to water-soluble copolymer, as argued by Applicant. Parker et al. disclosure clearly provides the teachings that the use of a macromolecular organic compound having a hydrophobic cavity, i.e. cyclodextrin, greatly reduces or eliminates the amount of gel formed during polymerization (See col. 7, lines 33-37). The fact that the compositions may be used to increase water repellency when applied to surfaces does not prevent said compositions from forming a hydrogel, once the cyclodextrin is removed.

8. In response to Applicant's argument, that Jodal et al. is silent with respect to applying cyclodextrin degradation in the area of polymer chemistry, it is noted that one of ordinary skill in the art would have been motivated to disrupt the interaction between the polymer and cyclodextrin in the compositions disclosed by Parker et al. by adding a molecule, such as α-amylase, with the expectation to induce formation of a hydrogel, in view of the teachings of Parker et al., that the presence of cyclodextrin in the polymer compositions reduces or inhibits the formation of a gel.

9. In reply to Applicant's argument, that Rhee et al. does not remedy the deficiencies of Parker et al. and Jodal et al., it is noted that the examiner relies on Rhee et al. only for the teachings that polymers compositions comprising cyclodextrin may include active proteins.

10. Applicant argues that Harmer et al. teaches a liquid form of fluorinated polymers and gelation refers to inorganic silica. In response to said argument, it is noted that the silicate composition disclosed by Harmer et al. is mixed with the fluorinated polymers before gelation (See col. 4, line 62 to col. 5, line 67). The comprising language of the claims in the instant application allows for additional ingredients in the compositions disclosed by the prior art. The method disclosed by Harmer et al. includes removing the organic solvent from the polymer composition and forming a gel, as claimed by Applicant.

Conclusion

11. Claims 1-21 are rejected.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

September 22, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600